

Amend independent claims 11 and 15 respectively, as recited hereinafter; and

Retain the language of previously presented dependent claims 13 and 14 respectively, as recited hereinafter.

In addition, in view of the explicit holdings of law rendered by the U.S. Supreme Court in the *Festo* case [*Festo Corp. v. Shoketsu kinzoku Kabushiki Co. Ltd. et al.*, 62 USPQ2d 1705 (2002)] concerning the applicability of the legal doctrine of equivalents to amended claim language, applicants now present a formal attestation and affirmation of the legal position and substantive rights:

Applicants do not now surrender for any reason, nor have previously surrendered at any time or for any reason during the prosecution of the instant application, any inventive subject matter which is or could be expected to be a particular equivalent of the invention defined by the language of the amended claims then pending as understood by a person of ordinary skill in this art; and that no presumption of estoppel, either in law or equity, exists or pertains now or at any time previously as a potential bar to the full application of the doctrine of equivalence for any and all possible embodiments which may be found to be encompassed now or in the future by the language of the amended claims proffered now or at any time

previously for substantive examination and review by the U.S. Patent Office. Accordingly, applicants hereby affirmatively rebut and explicitly dispute any presumption that the doctrine of equivalents for the language of the amended claims has been surrendered or is not in full force for any reason now and at any time during the prosecution on the merits of any and all claims defining the invention of the instant application.

Also, in accordance with the currently revised amendment practice (compulsory as of July 30<sup>th</sup>, 2003), applicants now present a listing and recitation of all the claims in ascending numerical order which were ever submitted for review; and include an identification of those cancelled or withdrawn claims which were previously submitted, as well as the full text of those claims currently pending in the instant application. The listing of all claims ever presented as well as the full text recitation of the presently pending claims begins on the immediately following page.

Claims 1-10 (canceled).

Claim 11 (currently amended). A PR-39 derived oligopeptide family whose members individually are operative and functional to cause a selective inhibition of proteasome-mediated degradation in-situ after introduction intracellularly to a viable cell, each member of said PR-39 derived oligopeptide family being:

a pharmacologically active peptide which is ~~less than 14~~ not substantially greater than 11 amino acid residues in length;

a pharmacologically active peptide whose N-terminal amino acid residue sequence begins with Arg-Arg-Arg;

a pharmacologically active peptide which is an analog of the amino acid sequence of native PR-39 peptide;

a pharmacologically active peptide operative selectively to alter the proteolytic degradation activity of proteasomes in-situ;

a pharmacologically active peptide operative selectively to interact in-situ with at least the  $\alpha 7$  subunit of such proteasomes as are present within the cytoplasm of the cell; and

a pharmacologically active peptide operative selectively to alter the proteolytic degradation activity of said proteasomes having an interacting  $\alpha 7$  subunit such that the proteolytic degradation mediated by said proteasomes against at least one peptide selected from the group consisting of NFkB

inhibitor I $\kappa$ B $\alpha$  and hypoxia-inducing factor (HIF)-1 $\alpha$  becomes selectively inhibited with substantially altering the proteolytic degradation of other peptides mediated by said proteasomes.

Claim 12 (canceled).

Claim 13 (previously presented). The PR-39 derived oligopeptide family as recited in claim 11 or 15 whose membership includes a peptide comprised of 11 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr-Leu-Pro-Arg (SEQ ID NO: 4).

Claim 14 (previously presented). The PR-39 derived oligopeptide family as recited in claim 11 or 15 whose membership includes a peptide comprised of 8 amino acid residues whose sequence is Arg-Arg-Arg-Pro-Arg-Pro-Pro-Tyr (SEQ ID NO: 5).

Claim 15 (currently amended). A PR-39 derived oligopeptide family whose members individually are operative and functional to cause a selective inhibition of proteasome-mediated degradation in-situ after introduction intracellularly to a viable cell, each member of said PR-39 derived oligopeptide family being:

a pharmacologically active peptide which is which is less than ~~14~~ 8 amino acid residues in length;

a pharmacologically active peptide whose N-terminal amino acid residue sequence begins with Arg-Arg-Arg;

a pharmacologically active peptide which is an analog of the amino acid sequence of native PR-39 peptide;

a pharmacologically active peptide operative selectively to alter the proteolytic degradation activity of proteasomes in-situ;

a pharmacologically active peptide operative selectively to interact in-situ with at least the  $\alpha 7$  subunit of such proteasomes as are present within the cytoplasm of the cell; and

a pharmacologically active peptide operative selectively to alter the proteolytic degradation activity of said proteasomes having an interacting  $\alpha 7$  subunit such that the proteolytic degradation mediated by said proteasomes against at least one peptide selected from the group consisting of NF $\kappa$ B inhibitor I $\kappa$ B $\alpha$  and hypoxia-inducing factor (HIF)-1 $\alpha$  becomes selectively inhibited with substantially altering the proteolytic degradation of other peptides mediated by said proteasomes.